National Marrow Donor Program®

Entrusted to operate the
C.W. Bill Young
Cell Transplantation Program

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August 05, 2008

Dr. Igor Vodyanoy
Office of Naval Research (ONR 342)
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: Quarterly Performance/Technical Report of the National Marrow Donor Program®

Reference: Grant Award #N00014-08-1-0058 between the Office of Naval Research and the National Marrow Donor Program

Dear Dr. Vodyanoy:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of April 1, 2008 to June 30, 2008.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention (612-362-3403 or at cabler@nmdp.org).

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Sr. Contracts Representative

Enclosure: Quarterly Report with SF298

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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation**:** Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

Grant Award N00014-08-1-0058

QUARTERLY
PERFORMANCE / TECHNICAL REPORT
FOR
APRIL 01, 2008 to JUNE 30, 2008

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
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QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

April 01, 2008 through June 30, 2008

TABLE OF CONTENTS

IIA. Contingency Preparedness – Hypothesis 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	
IIA.1.1 Aim 1: Secure Interest of Transplant Physicians	**Period 2 Activity:** No activity this period.
IIA.1.2 Aim 2: GCSF in Radiation Exposure	**Period 2 Activity:** No activity this period.
IIA.1 3 Aim 3: Patient Assessment Guidelines and System Enhancements	**Period 2 Activity:** **Research Sample Repository:** In the second quarter of 2008, the research repository software was upgraded. The main enhancements in this release were: • Enabling the repository staff to store new samples types (amplified DNA, RNA and • serum) • Changing processing protocols to simplify repository workflow • Reworked handling of related repository samples • Re-factored sample note processing and storage • Re-factored default vial calculations • Refined duplicate recipient processing rules. The software was successfully deployed at the repository, and is in usage by the repository staff. In June we released **CORD Link version 5.11,** which included the following: • A new action item was added to Workflow Management screen for the SCTOD (Stem Cell Therapeutic Outcomes Data) Data Form. The information will be passed to the CIBMTR for outcomes research. • CORD Link users now have the option to subscribe to Alerts in the CORD Link Application. Users simply add an email address under their user profile to request desired alerts notification for

search activity.

- The NMDP plans to replace Local ID with the recently implemented Full Local ID for all CBBs. Full ID Lookup will allow CBBs that are using the Full ID field to look up CBUs using their full ID. The Full Local ID eliminates the need for CBBs to truncate their ID numbers to fit into the ID field.
- Per FDA regulations, CORD Link was modified to include CMS laboratory certification status on the (Infectious Disease Marker) IDM questionnaire. The question is to be answered for all IDMs.

STAR Link features added in last period (Jan. 01 – Mar. 31, 2008) were:

- Search Screen Redesign – non-workup search requests
- Site Maintenance Redesign – Phase 1
- Kit Requests – add Assigned-to
- Updates feature
- New Donor Notes – works with Search notes
- New Security Permissions: Center Support Services, Recruitment, Help Desk
- Added "Willingness to Consider" field
- Added new Kit Request ship to location: Employer Address
- Added new "All" quick link from Work Flow Management Screen

STAR Link features added in this period **(April 01-June 30,2008)** were:

- Site Maintenance: Add Filters and Export
- Health History Questionnaire: Electronic STAR Link version
- E-mail link for Drive Detail Report
- SLQuery: Add query selector to handle merged centers
- Tracking Sheet changes: Remove Short version & add Long version with Notes
- Drive Screen, Recruiter field: Remove "Recruiter not Shown" option

IIA 1.4 Aim 4: National Data Collection Model	**Period 2 Activity:** • FormsNet v2.5 and v2.6 were released during the previous quarter providing a number of bug fixes and enhancements including imaging and improved tracking for forms due.
IIA. Contingency Preparedness – Hypothesis 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	
IIA.2.1 Aim 1: Contingency Response Network	**Period 2 Activity:** No activity this period.
IIA.2.2 Aim 2: Sibling Typing Standard Operating Procedures	**Period 2 Activity:** No activity this period
IIA. Contingency Preparedness – Hypothesis 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
IIA.3.1 Aim 1: I.S. Disaster Recovery	**Period 2 Activity:** • The data center relocation project has been completed and currently supporting the Enterprise Architecture initiatives which are underway. The next steps are to retro fit the coordinating center server room and to update the disaster recovery plan based on the relocation project.
IIA.3.2 Aim 2: Critical Facility and Staff Related Functions	**Period 2 Activity:** • During this period the Business Continuity Action Guide was created to provide guidance for NMDP operated facilities. This guide is a tool to assist managers of facilities, other than the Coordinating Center, with responding to crisis situations. Sections of the guide include: o Reporting what and when o Who to notify o Local hazards o How to prepare

	○ Hurricane ○ Flooding ○ Earthquake ○ Tornado ○ Winter storm ○ Power outage ○ Chemical spills ○ Extreme heat ○ Important contacts • The Business Continuity Planner conducted a site visit an NMDP operated center to work with staff in preparing to respond to a situation that may result in loss of access to the facilities, this included discussing all applicable areas of the Business Continuity Action Guide and entering appropriate information in the guide where needed. A site visit to the NMDP Leawood, KS facility was conducted this period.
IIB. Rapid Identification of Matched Donors – Hypothesis 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
IIB.1.1 Aim 1: Increase Registry Diversity	**Period 2 Activity:** No activity this period**.**
IIB.1.2 Aim 2: Evaluate HLA-DRB1 High Res typing	**Period 2 Activity:** This task is closed.
IIB.1.3 Aim 3: Evaluate HLA-C Typing of Donors	**Period 2 Activity:** This task is closed.
IIB.1.4 Aim 4: Evaluate Buccal Swabs	**Period 2 Activity:** No activity this period.

IIB 1.5 Aim 5: Enhancing HLA Data for Selected Donors	**Period 2 Activity:** No activity this period.
IIB 1.6 Aim 6: Maintain a Quality Control Program	**Period 2 Activity:** No activity this period.
IIB. Rapid Identification of Matched Donors – Hypothesis 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
IIB 2.1 Aim 1: Collection of Primary Data	**Period 2 Activity:** • A new SBT reporting format that includes gSSP results (ambiguity resolution using SBT) was proposed. Interpretation of SBT is implemented as a up-front technique • Development of new reporting formats that meet the needs of the HIEDFS (HLA Information Exchange Data Format Standards) consortium continued during the past quarter with an in-person meeting at the EFI conference to review the draft standard and make enhancements
IIB 2.2 Aim 2: Validation of Logic of Primary Data	**Period 2 Activity:** This task is closed.
IIB 2.3 Aim 3: Reinterpretation of Primary Data	**Period 2 Activity:** This task is closed.
IIB 2.4 Aim 4: Genotype Lists & Matching Algorithm	**Period 2 Activity:** No activity this period.

IIB. Rapid Identification of Matched Donors – Hypothesis 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
IIB.3.1 Aim 1: Phase I of EM Haplotype Logic	**Period 2 Activity:** No activity this period.
IIB 3.2 Aim 2: Enhancement of EM Algorithm	**Period 2 Activity:** • A manuscript entitled "Re-creation of the Genetic Composition of a Founder Population" was submitted to Human Genetics • A manuscript entitled "The HLA genetics of Jewish populations" was drafted and forwarded to the writing committee for submission during the next quarter • Three abstracts were submitted to ASHI (2 accepted for poster, 1 for oral presentation) on haplotype analysis • Three abstracts were submitted to the 15th IHIWS conference ("High resolution reconstruction of HLA haplotypes in Native Americans", "HLA haplotype diversity in Brazil" and "Anthropological Insights from a Novel Visualization and Clustering Tool for HLA Haplotypes and Populations"
IIB 3.3 Aim 3: Optimal Registry Size Analysis	**Period 2 Activity:** • Study design work has progressed on the clinical validation of 8/8 matching. • A random set of Caucasian donors, to be used as pseudo-patients, has been selected and sent for typing for this study
IIB 3.4 Aim 4: Target Under-represented Phenotypes	**Period 2 Activity:** • GIS (Geographical Information System) Software has been selected (ESRI) for use in generating true geographical encoding of donors under this aim • A model of genetic diversity (based on census population within recruitment regions) was proposed and accepted as part of the 5 year recruitment plan for measuring diversity goals

	• A second phase of GIS software selection is underway which will include the ability to provide in-house address validation according to the statement of work for this aim.
IIB 3.5 Aim 5: Bioinformatics Web Site	**Period 2 Activity:** This task is closed.
IIB 3.6 Aim 6: Consultants to Improve Algorithm	**Period 2 Activity:** No activity this period.
IIB. Rapid Identification of Matched Donors – Hypothesis 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
IIB.4.1 Aim 1: Expand Network Communications	**Period 2 Activity:** SEARCH Link™ application upgrades • Donor Information Infectious Disease Markers (IDMs) screen and Donor Information Report • Added additional tests: Chagas (screening) and Chagas (confirmatory), along with their results and test dates performed • Revisions to the Form 24 v12.0 and Form 50 v13.0 resulted in: o Text change for CMV Total to Anti-CMV Total o Results changed for Anti-CMV Total from Not Performed, Positive, Negative, and Prev. Positive to Not Performed, Reactive, Non-reactive, and Prev. Reactive o Interpretation of IDM test results was changed from "Interpretation information for infectious disease marker (IDM) testing is available on the NMDP Network Website" to "Interpretation information for infectious disease marker (IDM) test results is available on the NMDP Network Web site." o Cord Information Maternal Infectious Disease Marker screen and Cord Information (Detailed and Summary) and Cord Lab Summary Reports o The Chagas EIA test text was changed to Chagas (screening) o The RIPA (confirmatory) test was changed to Chagas (confirmatory)

- Restored the display of Release Codes for released donors on the Potential Donor List and 110A reports
- Electronic Workup
  - Validation rules for the Day of Collection Samples section was added as follows:
    - If marrow and/or PBSC is requested or patient is on PBSC vs. Marrow randomized trial, the tubes of peripheral blood listed under Day 1(marrow and PBSC) must total at least 7 ml when added together.
    - If PBSC is requested or patient is on PBSC vs. Marrow randomized trial, the tubes of peripheral blood listed under Day 2(PBSC only) must total at least 7 ml when added together.
  - A pop-up warning was added to display when the selected source could be one and the same as the patient based on birth date, sex, and match grades

The TRANS Link® application was retired on May 31, 2008. *Future reporting will only be under the Traxis application.*

- Traxis™ application was released in production March 17th, 2008. Traxis is the NMDP's fully-integrated search management interface. This web-based application is used by transplant centers to manage and track the entire search process, to access unrelated adult donors and cord blood units worldwide, from initial search to transplantation. Traxis combines multiple functions, allowing users to perform searches, request HLA typing, manage their workflow, request work-ups and perform multi-cord searches. Traxis incorporates a host of time-saving features designed to improve accuracy and simplify the search management process. It offers the electronic workup or cord order request feature and a better user interface. This application replaced the current TRANS Link application.
- 137 centers, both domestic (123) and international (14), comprising 325 users have switched from the old TRANS Link application to the new Traxis application.

Traxis was upgraded on June 14th to fix defect and performance issues identified during the first two months of use.

	STAR II upgrades: • Star2 build 052 deployed 2008-04-09 o Support for Sample QCSW (Quality Control Software) transactions from NMDP repository. This was required for removing dependency from 'Tracking Tables' in the 'Star DB'. The feature is now implemented on Star II. • Star2 build 053 deployed 2008-05-20 o Performance improvement to reduce the time required to aggregate XML transactions into a document and send as e-mail. This will reduce the time to distribute transaction files sent to CordLink, StarLink and other XML enabled applications.
IIB.4.2 Aim 2: Central Contingency Management	**Period 2 Activity:** No activity this period.
IIB.4.3 Aim 2: Benchmarking Analysis	**Period 2 Activity:** This task is closed.
IIB.4.4 Aim 2: Expand Capabilities of Collection and Apheresis Centers	**Period 2 Activity:** No activity this period.
IIC. Immunogenetic Studies – Hypothesis 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
IIC.1.1 Aim 1: Donor Recipient Pair Project	**Period 2 Activity:** • Support for Sample groups 19 and 20 of the donor/recipient HLA research project is ongoing • Development of the ability to process primary data for this project is underway under this aim (to be included as part of the IPR database IIC 2.1)

IIC. Immunogenetic Studies – Hypothesis 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
IIC 2.1 Aim 1: Analysis of non-HLA loci	**Period 2 Activity:** • Continued development of the IPR (Immunobiology Project Results) database occurred during the past quarter. This database will replace the existing HLA donor/recipient pairs database and have the capacity to process KIR, SNPs, or any other Immunobiological tests. Input file (HML) processing has been developed and the analysis of processing rules (lab-to-lab comparison, ambiguity analysis, data audits) is nearing completion. The development is on track to deliver the IPR database in time for the SG21 which includes both HLA and KIR typing for research.
IIC 2.2 Aim 2: Related Pairs Research Repository	**Period 2 Activity:** No activity this period.
IID. Clinical Research in Transplantation – Hypothesis 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
IID.1.1 Aim 1: Observational Research, Clinical Trials and NIH Transplant Center	**Period 2 Activity:** No activity this period.
IID.1.2 Aim 2: Research with NMDP Donors	**Period 2 Activity:** No activity this period.
IID.1.3 Aim 3: Expand Immuno-biology Research	**Period 2 Activity:** No activity this period.

ACRONYM LIST

AABB	American Association of Blood Banks	IND	Investigational New Drug
AML	Acute Myelogenous Leukemia	ICRHER	International Consortium for Research on Health Effects of Radiation
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IS	Information Services
ASBMT	American Society for Blood and Marrow Transplantation	IT	Information Technology
ASHI	American Society for Histocompatibility and Immunogenetics	IRB	Institutional Review Board
B-LCLs	B-Lymphoblastoid Cell Lines	KIR	Killer Immunoglobulin-like Receptor
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	NCI	National Cancer Institute
BRT	Basic Radiation Training	MHC	Major Histocompatibility Complex
C&A	Certification and Accreditation	MICA	MHC Class I-Like Molecule, Chain A
CBMTG	Canadian Blood and Marrow Transplant Group	MICB	MHC Class I-Like Molecule, Chain B
CBB	Cord Blood Bank	MUD	Matched Unrelated Donor
CBC	Congressional Black Caucus	NCBM	National Conference of Black Mayors
CBS	Canadian Blood Service	NIH	National Institutes of Health
CBU	Cord Blood Unit	NIMS	National Incident Management System
CHTC	Certified Hematopoeitic Transplant Coordinator	NK	Natural Killer
CIBMTR	Center for International Blood & Marrow Transplant Research	NMDP	National Marrow Donor Program
CLIA	Clinical Laboratory Improvement Amendment	NRP	National Response Plan
CME	Continuing Medical Education	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
COG	Children’s Oncology Group	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CREG	Cross Reactive Groups	OIT	Office of Information Technology
CT	Confirmatory Testing	OMB	Office of Management and Budget
CTA	Clinical Trial Application	ONR	Office of Naval Research

DIY	Do it yourself	PBMC	Peripheral Blood Mononuclear Cells
DKMS	Deutsche Knochenmarkspenderdatei	PBSC	Peripheral Blood Stem Cell
DMSO	Dimethylsulphoxide	PCR	Polymerase Chain Reaction
DNA	Deoxyribonucleic Acid	PSA	Public Service Announcement
D/R	Donor/Recipient	QC	Quality control
EBMT	European Group for Blood and Marrow Transplantation	RCC	Renal Cell Carcinoma
EM	Expectation Maximization	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
EMDIS	European Marrow Donor Information System	REAC/TS	Radiation Emergency Assistance Center/Training Site
FBI	Federal Bureau of Investigation	RFP	Request for Proposal
FDA	Food and Drug Administration	RFQ	Request for Quotation
Fst	Fixation Index	RITN	Radiation Injury Treatment Network
GETS	Government Emergency Telecommunications Service	SBT	Sequence Based Typing
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	SCTOD	Stem Cell Therapeutics Outcome Database
GvHD	Graft vs Host Disease	SG	Sample Group
HHS	Health and Human Services	SSP	Sequence Specific Primers
HIPAA	Health Insurance Portability and Accountability Act	SSOP	Sequence Specific Oligonucleotide Probes
HLA	Human Leukocyte Antigen	STAR®	Search, Tracking and Registry
HML	Histoimmunogenetics Mark-up Language	TC	Transplant Center
HR	High Resolution	TED	Transplant Essential Data
HRSA	Health Resources and Services Administration	TNC	Total Nucleated Cell
HSC	Hematopoietic Stem Cell	TSA	Transportation Security Agency
IBWC	Immunobiology Working Committee	URD	Unrelated Donor
IDM	Infectious Disease Markers	WMDA	World Marrow Donor Association
IHWG	International Histocompatibility Working Group	WU	Work-up